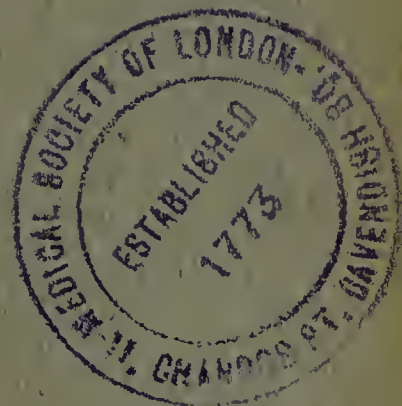


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MAN AT REST AND AT WORK

THE REGULATION OF THE CIRCULATION



BY
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Hospital, Boston, Mass.*

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CLINIC OF PROFESSOR CUSHING

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Bornstein¹ in 1910 introduced the principle of measuring the volume of blood per minute passing through the lungs of man by calculating, from the tension difference existing between the gas (nitrogen) in the alveolar air and in the blood, the quantity absorbed by the blood from the lungs in a known time. The next year Markoff, Muller, and Zuntz² improved the method by using nitrous oxide instead of nitrogen.

Krogh and Lindhard³ in 1912 nearly coincidently with Markoff, Muller, and Zuntz employed nitrous oxide and developed the method to a high degree of accuracy. Krogh⁴ has recently shown, however, that an error of the order of about 6 per cent exists in all the blood flow experiments given in the above paper, as well as in recent papers by Lindhard,⁵ because in the calcula-

¹ Bornstein: Eine Methode zur vergleichenden Messung des Herzschlagvolumens beim Menschen. *Pflugers Archiv* 1910, cxxxii, pp. 307-318.

² Markoff, Muller, and Zuntz: Eine Stickoxydul-Methode zur Bestimmung der umlaufenden Blutmenge in lebenden Körper. *Ztschft. f. Balneologie*, 1912, iv, 14-15.

³ Krogh and Lindhard: Measurement of the blood flow through the lungs of man. *Skand. Archives f. Physiol.*, 1912, xxvii, pp. 100-125.

⁴ Krogh: Funktionsuntersuchungen an den Lungen des Menschen mittelst gasanalytischer Methoden; Abderhalden: *Handbuch der Biochem. Arbeitsmethoden*. 1915, Urban und Schwarzenberg. pp. 550-558.

⁵ Lindhard: Concerning the influence of ultraviolet light on the circulation in man. *Skand. Archives f. Physiol.*, 1913, xxx, pp. 73-96; Lindhard: Effect of posture on the output of the heart. *Skand. Archiv. f. Physiol.*, 1913, xxx, 395-408.

tions the coefficient of absorption of nitrous oxide for blood has been taken as 0.43, as determined by Siebeck in 1909 for ox blood at 37°. Lindhard and Krogh⁶ have recently determined the coefficient of absorption of nitrous oxide for human blood at 37° and found it to be 0.405 ± 0.005 .

The method used by us in the present study is essentially that given by Krogh in his most recent paper.⁷ However, as a few changes in the routine of experimentation have been made by us we present our technic in full.

EXPERIMENTAL DETAILS

Unit of work. The object of our experiments is to show the volume per minute of the circulation between a condition of complete rest in bed to one of severe muscular work. It was necessary to have a method of expressing the amount of work performed by the subject under all the conditions of the experiments. A mechanical unit, such as kilogram-meters per minute, gives a rough comparative idea of the amount of work performed by the subject while pedaling an ergometer, such as that described by Krogh.⁸ This unit, however, cannot be used to compare the amount of work a subject's muscles would be called upon to perform when sitting at rest on a bicycle, in a chair, or lying in bed; further, it does not take into consideration variations produced in efficiency by a proper position on the seat or the energy expended by the arm muscles exerting a counter pull on the handle bars of the bicycle. We have, therefore, adopted the physiological unit of the number of cubic centimeters of oxygen consumed per minute.

For the study of the circulation rate, the unit of oxygen consumption per minute is particularly well adapted, for it is one of the chief functions of the blood to transport the gases between the lungs and tissues. In fact the transportation of the other metabolic substances of the blood current, though equally essen-

⁶ Krogh: See reference 4, p. 550.

⁷ Krogh: See reference 4.

⁸ Krogh: A bicycle ergometer and respiration apparatus for the experimental study of muscular work. Skand. Archiv. f. Physiol., 1913, xxx, 375-394.

tial to the organism, are probably comparatively small from the point of view of bulk per unit volume of blood, though of great importance from the point of view of their effect on the gaseous carrying capacity of a unit volume of blood.

Body equilibrium. The gaseous equilibrium of the body for the condition of the experiment is established by having the subject maintain such a condition of rest or of work for at least one-half hour before any experimental observations are made.

Rest. For the experiments at complete rest, the subject lay on his back in bed without moving throughout the entire preliminary and experimental periods. The various mouthpieces were supported on a bar, and the necessary manipulations of changing from one to another were performed for him. The experiments were usually done about the middle of the forenoon after an ordinary breakfast. It was not considered necessary to insist on a basic, fasting condition, as the study was not the determination of the lowest possible circulation rate but the volume per minute of blood necessary to transport a unit volume of oxygen. In fact a slight variation from day to day in the oxygen consumption would be advantageous as it might reveal corresponding changes in the blood flow. In addition to the experiments at complete rest others were done with the subject seated in a straight-backed chair; otherwise no change in the routine was made.

Work. For the work experiments a stationary bicycle with the rear wheel heavily balanced by a lead pipe tire and suitably mounted was used. The degree of work performed by the subject was regulated by changing the resistance of a friction brake, or by varying the speed of pedaling. During a single experiment, including the preliminary period for establishing equilibrium, the brake resistance and the rate of pedaling were maintained constant, the latter was accomplished by pedaling in time to the ticking of a metronome.

Respiratory exchange. The oxygen consumption per minute was determined by making a complete respiratory exchange

experiment after equilibrium was established and just before the circulation experiment proper. The subject breathed through a set of Douglas valves into a 30-litre collecting spirometer. The surfaces of the valve-discs were covered with a layer of thick machine oil; in addition, a small loop of wire was passed around the cross wires over the valve-disc and the free end rested on the disc increasing its weight slightly. These changes reduced the leakage below an appreciable point without noticeably increasing the resistance to the passage of air.

The spirometer was carefully calibrated and the air volumes could be determined within 50 cc. an error of 0.2 per cent for 25 litres. The air samples were analyzed in a regular 10 cc. Haldane⁹ gas analysis apparatus, the error of which for routine work does not exceed 0.02 per cent. The duration of the respiration experiment was obtained by a stop-watch and determined to a fifth of a second, which would give an error of 0.05 per cent for the rest and 0.3 per cent for the work experiments. The tap was turned at the bottom of expiration both at the beginning and at the end of an experiment. The carbon dioxide elimination and the oxygen consumption per minute were calculated in the usual way, allowing for the change in volume of the expired air.¹⁰ To avoid the necessity of making a correction for the dead space of the spirometer it was filled with expired air and then emptied just before beginning the experiment.

Temperatures. The temperature of the gas in the collecting and recording spirometers was taken as that of the water bath at the time of measurement of the gas volume and read to 0.1°C. and the gas was assumed to be fully saturated with water vapor. The temperature of the gas in the lungs and air-passages was taken as 37°, and likewise assumed to be fully saturated with water vapor.

Barometer. The atmospheric pressure was determined by a mercury barometer of the U. S. Weather Bureau type and read by means of a vernier to 0.1 mm. The observed reading was

⁹ Haldane: Methods of air analysis. 1912, Charles Griffin & Co., London.

¹⁰ Haldane: Methods of air analysis (p. 56). 1912, Charles Griffin & Co., London.

always corrected to 0°C. The barometer was read at the time of measuring of the gas volumes.

Pulse rate. To obtain the pulse rate both at the time of the respiration and circulation experiments, an ordinary 6-inch clinical blood pressure cuff was placed on the subject's arm. The cuff was inflated to a point just above the diastolic blood pressure and was connected to a tambour or mercury manometer which wrote on the kymograph under the tracing made by the recording spirometer. The cuff could be worn with comfort for periods as long as fifteen minutes.

Recording spirometer. A carefully calibrated 6-litre Krogh recording spirometer was used to contain the nitrous oxide mixture. From the spirometer curve it was possible to read the volumes with an average error not exceeding 10 cc. and as the differences in volume were more than 1000 cc. the error was less than 1.0 per cent. To insure the thorough mixing of the gases a small fan on the floor of the spirometer was kept running throughout an experiment by means of a small electric motor.

The preliminary gas mixture was made by introducing into the spirometer 4.5 L. of air, 0.5 L. of oxygen, and 1.0 L. of nitrous oxide. After thorough mixing the mouth tap was opened so as to fill this and the connecting tube with the mixture.

A piece of garden hose of 20 mm. inside diameter and about 20 cm. long led from the spirometer to a three-way brass valve to which was attached a rubber mouthpiece with a wide flange that fitted in between the lips, cheeks, and teeth. By means of this valve the subject could be connected either with the spirometer, or the outside air, or the valve could be entirely closed. To the spirometer side of the valve was connected a flexible lead tube of 0.6 mm. bore by means of which alveolar air samples could be withdrawn into collecting tubes.

In the circulation experiments the time is written on the drum in seconds and can be read with an error not exceeding 0.1 seconds which would give for an experiment of 20 seconds an error of 0.5 per cent.

Analysis of nitrous oxide. The analysis of the dilute nitrous oxide mixture is accurate in routine work to within 0.05 per

cent. If exceptional care is taken with an absolutely clean burette the percentages can be determined to within an error of 0.03 per cent. As the studies here presented are based on the accuracy of the nitrous oxide analyses we felt obliged, as a preliminary step, to satisfy ourselves of the fundamental accuracy of the analytical technic and the results of our studies are presented in a separate article.¹¹

Residual air. As the volume of the subject's residual air is necessary in making the calculation of the total volume of the nitrous oxide mixture in the lungs, this must be determined by preliminary experiments. This we did by the usual hydrogen method the details of which need not be given here. Unlike Krogh,¹² we could find no difference in the volume of the residual air whether at rest or at work, therefore we have used the same volume in the calculation of all our experiments. We are planning to elaborate on this point in a separate article.

The circulation experiment proper. The mouthpiece of the recording spirometer is adjusted in the subject's mouth so that it will be air-tight, and the nose is closed with a clip. The subject breathes through this valve to the room air for two or three minutes being careful to maintain the same rate of pedaling in the work experiments or to keep absolutely quiet in the rest experiments. On signal he gives the greatest possible expiration at the end of which the observer turns the tap so that the following inspiration consists of the nitrous oxide mixture in the spirometer. When the subject has inspired an easy maximum, the observer closes the tap so that the subject holds his breath for five to eight seconds, in order that the lung tissues and the blood already in the lungs may reach an equilibrium with the tension of the nitrous oxide in the alveolar air. Then the observer opens the tap to the spirometer and the subject gives a sharp expiration of such a volume that he expires as near as possible to his "Mittelage." The observer closes the tap and the subject holds his breath for fifteen to twenty seconds.

¹¹ Boothby and Sandiford: The analysis of nitrous oxide for physiological work. This Journal, 1915, xxxvii.

¹² Krogh: See reference 4, pp. 536-539.

As soon as the tap is closed the observer withdraws a sample of the expired air (Sample No. 1). Then on signal the observer again opens the tap to the spirometer and the subject expires very deeply and quickly; the tap is then turned to the room air, and a sample of the second expiration is taken (Sample No. 2).

It seems reasonable to assume *under constant conditions of metabolism*, that the gaseous content of the venous blood as it enters the lungs does not appreciably vary from moment to moment. However, during an experiment in which the breath is held marked changes would naturally follow if any part of the total blood volume could during this time effect a complete circuit and reenter the lungs a second time. The probability of the presence of recirculating blood would depend on the relationship between the total blood volume and the rapidity of the circulation rate. The blood volume of the subject of these experiments has never been determined but judging from the figures given by Douglas,¹³ it cannot be far from 3.8 L., allowing for the difference in weight. As the duration of the experiments at rest does not exceed twenty-five to thirty seconds and at work fifteen to eighteen seconds, and as the circulation rate under corresponding conditions is 3.4 and 9.3 litres per minute respectively, it is extremely unlikely that any blood would have time to return to the lungs except that of the coronary circulation. This latter would be of such a relatively small amount that no serious error is probably introduced by neglecting it.

The abnormal condition of the subject while holding his breath during the circulation experiment affects the blood flow markedly by altering the intrapulmonary air pressure. If this air pressure is high, less blood will tend to flow into the thoracic cage than if the air pressure is low. The amount of this variation in intrapulmonary pressure can in large part be obviated by making the expiration after the preliminary period of such a volume that the chest walls are in a position of elastic equilibrium;

¹³ Douglas: The determination of the total oxygen capacity and blood volume at different altitudes by the carbon monoxide method. Jour. Physiol., 1910, xl, 6, 471-478.

this position corresponds to the bottom of a normal expiration. Furthermore, the subject must not hold his thoracic muscles rigid during the experimental period because the volume of air in the lungs is decreasing; in consequence, the chest wall must

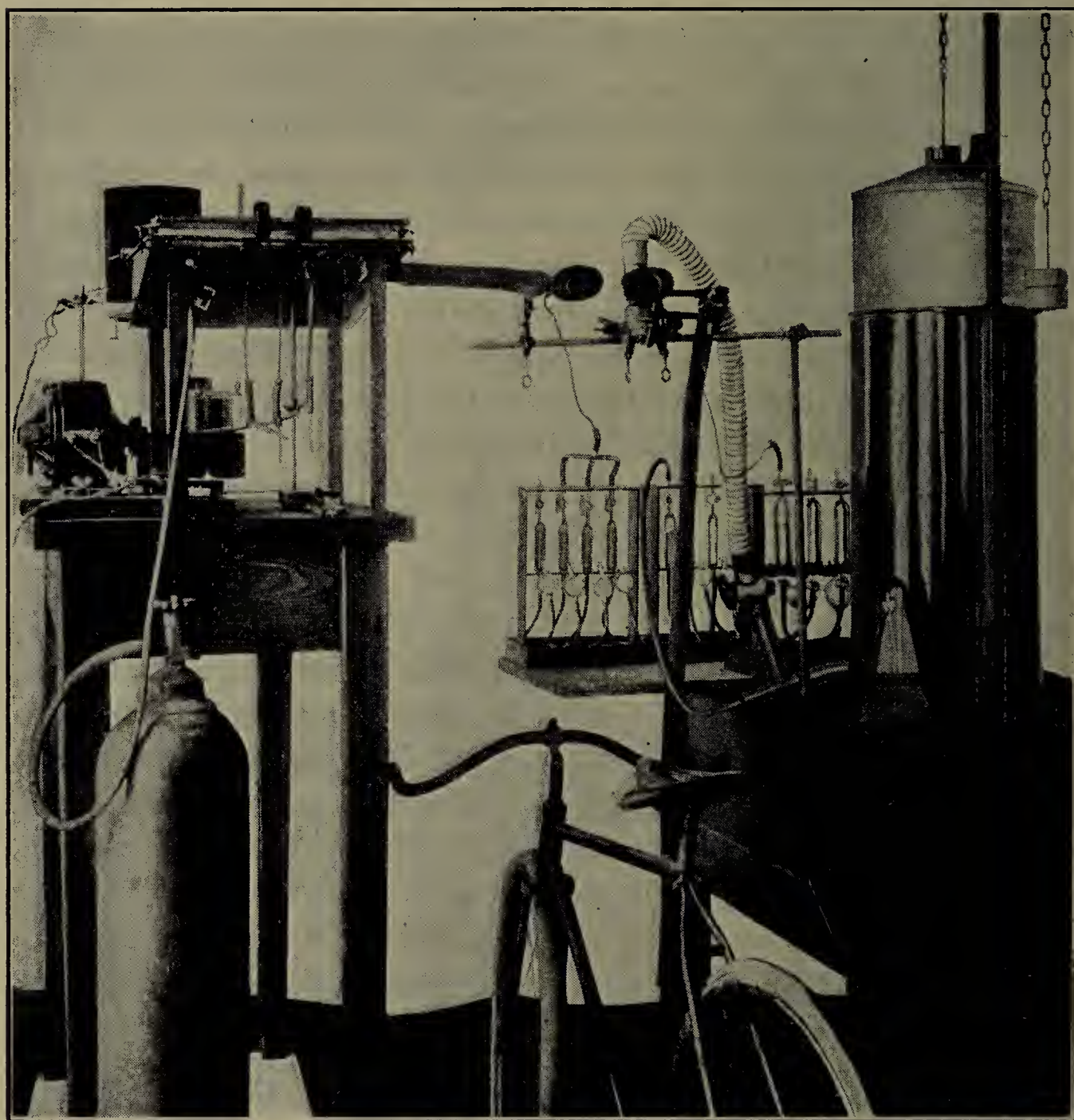


Fig. I. Arrangement of the apparatus for respiration and circulation experiments at work.

be allowed to contract down proportionately, otherwise a negative intrapulmonary pressure would be developed, thereby sucking into the lungs an excess amount of blood.

In practice it is impossible to expire to the exact position of

elastic equilibrium therefore more or less blood may flow into the lungs on account of the disturbed pressure conditions inside the thorax than would normally flow under the metabolic conditions of the experiment. From the circulation experiment proper it is possible to determine the oxygen absorbed by the blood; by means of the preliminary respiration experiment under identical metabolic conditions the normal oxygen consumption for these conditions is known. Therefore as the oxygen content of the venous blood during an experimental period is constant, the difference in oxygen consumption will be proportional to the difference in the volume of the blood entering the lungs. In consequence the observed minute volume can be corrected by dividing it by the oxygen absorption found in the circulation experiment and then multiplying the result by the oxygen absorption determined in the preliminary respiration experiment (see protocol of circulation experiment).

PROTOCOL OF EXPERIMENT

Experiment No. 7, May 9, 1914; Subject, W. M. B., resting on bed.

Respiratory exchange experiment

Prelim. period.....30 min.	Bar.....755.3
Duration of exp....6.3 min.	Corr. Temp..... 2.8
Temp. spir.....22.5°	Corr. Bar.....752.5
	Temp. bar 23.0°
Reading spir.—End..... 29.40 L.	
Reading spir.—Start..... 0.38 L.	
Total volume..... 29.02 L. at 752.5 and 22.5° sat.	
or..... 25.82 L. at 760 and 0° dry.	

Analysis of air samples from the spirometer, in duplicate

<i>Sample 1</i>	<i>Sample 2</i>
9.407	9.499
Sample...9.407	9.499
9.083	9.173
CO ₂9.083 = 0.324 = 3.44 per cent	9.173 = 0.326 = 3.43 per cent
7.492	7.565
O ₂7.492 = 1.591 = 16.91 per cent	7.565 = 1.608 = 16.93 per cent

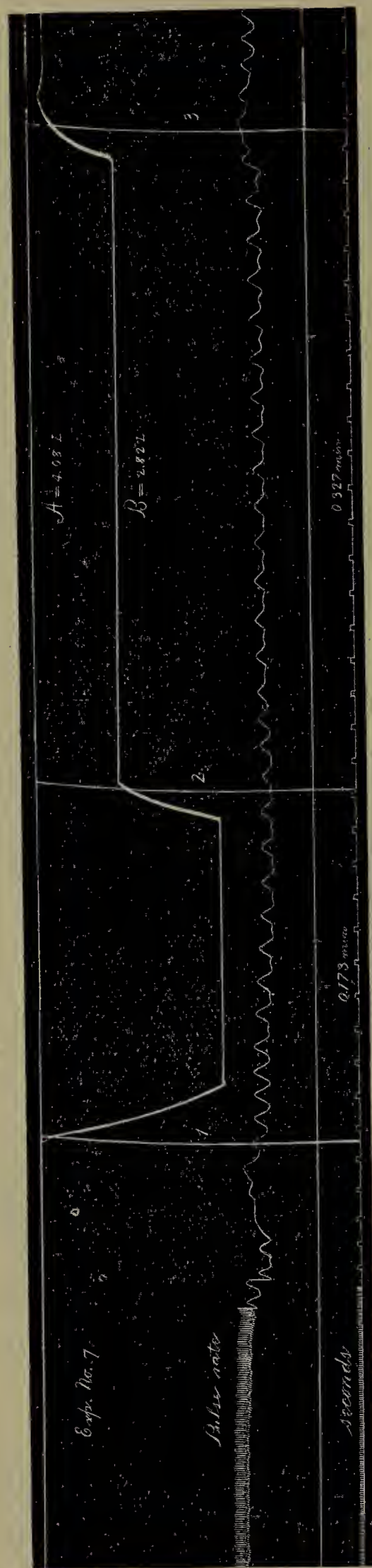


Fig. II. Spirometer and pulse tracing of experiment No. 7, May 9, 1914. See protocol.

$$\text{CO}_2 = 3.44 \text{ per cent}$$

$$\text{O}_2 = 16.92 \text{ per cent}$$

$$\text{N}_2 = 79.64 \text{ per cent}$$

$$20.93 \times \frac{79.64}{79.04} = 21.09 \text{ per cent}$$

CO₂ eliminated.

$$3.44 - 0.03 = 3.41;$$

$$\frac{3.41}{100} \times 25.82 = 880 \text{ cc. for 6.3 min.}$$

or 140 cc. per min.

O₂ Absorbed.

$$21.09 - 16.92 = 4.17;$$

$$\frac{4.17}{100} \times 25.82 = 1077 \text{ cc. for 6.3 min.}$$

or 171 cc. per min.

$$\text{Resp. quo.} = \frac{140}{171} = 0.819$$

$$\text{Ventilation per minute} = \frac{25.82}{6.3} = 4.10 \text{ L at 760 and } 0^\circ \text{ dry}$$

or 5.01 L at 760 and 37° sat.

Circulation experiment proper

Introd. period. 10.4 secs. = 0.173 min.	Bar. 755.3
Exper. period. 19.6 secs. = 0.327 min.	Corr. Temp. 2.8
Temp. spir. 21.8°	Corr. Bar. 752.5
	Temp. bar. 23.0°

Analysis of samples

<i>Sample 1</i>	<i>Sample 2</i>
9.393	9.393
Sample. . . . 9.393	9.393
CO ₂ 8.983 = 0.410 = 4.37 per cent	8.833 = 0.560 = 5.96 per cent
O ₂ 7.619 = 1.364 = 14.52 per cent	7.693 = 1.140 = 12.14 per cent
Adding H ₂ . 9.409	9.367
9.409	9.367
8.183	8.352
N ₂ O. 8.183 = 1.226 = 13.05 per cent	8.352 = 1.015 = 10.81 per cent
N ₂	68.06 per cent
	71.09 per cent

Vol. air in spir. at end of exp.....	4.08 L (see Fig. II)
Vol. air in spir. during exp.	<u>2.82 L (see Fig. II)</u>
Vol. air in lungs during exp.....	1.26 L
Vol. alv. resid. air.....	<u>1.10 L</u>
Total vol. in lungs during exp.....	2.36 L

Corrections:

$$\text{Sample 1} = 25 \text{ cc.}$$

$$6 \times 10.4 = \underline{62 \text{ cc.}}$$

$$87 \text{ cc.} = \underline{0.09 \text{ L}}$$

$$\text{Vol. air in lungs at start of exp.....} \underline{2.27 \text{ L}}$$

$$\text{Vol. air in lungs at end of exp... } 2.27 \times \frac{68.06}{71.09} = 2.17 \text{ L.}$$

O₂ Absorbed

$$2.27 \times \frac{14.52}{100} = 0.3296 \text{ L}$$

$$2.17 \times \frac{12.14}{100} = \underline{0.2634 \text{ L}}$$

0.0662 L at 752.5 and 21.8° sat.

or 0.0591 L at 760. and 0° dry.

$$\frac{0.0591}{0.327} = \underline{181 \text{ cc. per min.}}$$

N₂O Absorbed.

$$2.27 \times \frac{13.05}{100} = 0.2962 \text{ L}$$

$$2.17 \times \frac{10.81}{100} = \underline{0.2346 \text{ L}}$$

0.0616 L at 752.5 and 21.8° sat.

or 0.0550 L at 760. and 0° dry.

$$\frac{13.05 + 10.81}{2} = 11.93 \text{ per cent}$$

$$11.93 \times \frac{753-47}{760} = 11.93 \times \frac{706}{760} = 11.08 \text{ per cent}$$

Blood flow.

$$\frac{0.0550}{0.405 \times 0.1108 \times 0.327} = 3.75 \text{ L}$$

Blood flow corrected to normal exchange.

$$3.75 \times \frac{171}{181} = \underline{3.54 \text{ L}}$$

THE CALCULATION OF AN EXPERIMENT

The various steps in the calculation of an experiment have been given above in the protocol, most of which are self-evident. Several points in the calculation of the blood flow need, however, further elucidation.

The nitrogen percentage in Sample 2 has risen during the experiment and is due, as Krogh and Lindhard point out, to a

slight liberation of nitrogen from the blood as well as to the contraction in volume of the air in the lungs because of the absorption of oxygen and nitrous oxide that is only partly offset by the elimination of carbon dioxide. The amount of nitrogen liberated from the blood is so small that it can be neglected, as Krogh and Lindhard have shown.

The volume of air from the spirometer curve is of course equal to the difference between *A* and *B* (see Fig. II). From other experiments we know the subject's alveolar residual air to be 1000 cc. (at 760 and 0° dry), and have corrected this for an average experimental temperature of 22.0°. Where there are great variations in experimental temperature from 22.0°, we have recalculated the residual air for that temperature.

The correction for the change in volume of the air in the lungs during the introductory period is calculated from that found in the experimental period. The volume of the air in the lungs at the end of the experiment is calculated from the percentage of nitrogen in the two samples:

$$2.27 \times \frac{68.06}{71.09} = 2.17 \text{ L.}$$

The contraction in volume of the air during the experimental period is therefore $2270 - 2170 = 100$ cc. in 19.6 seconds. Or the change in volume per second is 5 cc. The contraction in volume of the air during the introductory period is taken to be the same as that during the experimental period. Krogh has taken it to be 6 cc. per second and we have found this a fair average for the rest experiments. In work, however, the volume change per second varies considerably and we have, therefore, calculated the value for each of the work experiments.

To determine the duration of the introductory and experimental periods lines are dropped from the respiration curve to the time curve. In doing this allowance must be made for the dead space as the instant at which the sample obtained actually left the lungs preceded the completion of the expiration by the time requisite for this volume of air to be expired. By other experiments we determined that the combined dead space of the subject and the valve was 125 cc.

The quantity of N_2O in the lungs at the beginning of the experimental period is

$$2.27 \times \frac{13.05}{100} = 0.2962 \text{ L.}$$

At the end of the period it is

$$2.17 \times \frac{10.81}{100} = 0.2346 \text{ L.}$$

The quantity of N_2O absorbed is

$$\begin{array}{l} 0.2962 \text{ L.} - 0.2346 \text{ L.} = 0.0616 \text{ L. at } 752.5 \text{ and } 21.8^\circ \text{ sat.} \\ \text{or} \qquad \qquad \qquad 0.0550 \text{ L. at } 760 \text{ and } 0^\circ \text{ dry.} \end{array}$$

The mean percentage of N_2O in the lungs can be taken as

$$\frac{13.05 + 10.81}{2} = 11.93 \text{ per cent}$$

Or, expressed in per cents of an atmosphere (dry)

$$11.93 \times \frac{753 - 47}{760} = 11.93 \times \frac{706}{760} = 11.08 \text{ per cent}$$

The absorption coefficient of N_2O at 37° is 0.405 (Lindhard and Krogh.¹⁴) Therefore the volume of blood necessary to absorb 0.0550 L. of N_2O is

$$\frac{0.0550}{0.405 \times 0.1108} = 1.23 \text{ L.}$$

And this volume must have passed through the lungs during the 0.327 minutes of the experiment. Therefore the minute volume equals

$$\frac{1.23}{0.327} = 3.75 \text{ L.}$$

The oxygen absorbed during the circulation experiment proper is calculated in the same manner as that of the N_2O (see protocol).

From the spirometer experiment preceding the blood flow experiment the oxygen absorbed per minute was found to be 171 cc. The corrected blood flow is therefore

¹⁴ Krogh: See reference 4, p. 550.

$$3.75 \times \frac{171}{181} = 3.54 \text{ L.}$$

Instead of reducing the volume of air in the lungs, Krogh corrects the percentages in the second sample to what they would have been had the volume remained the same. The above analyses would have been corrected thus.

	Sample 1	Sample 2	Sample 2 Corr.	1-2 Corr.	$\frac{1+2}{2}$
	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
CO ₂	4.37	5.96	5.71		
O ₂	14.52	12.14	11.62	2.90	
N ₂ O	13.05	10.81	10.35	2.70	11.93
N ₂	68.06	71.09			

The blood flow is then calculated as follows:

$$\frac{2.27 \times 0.0270}{0.405 \times 0.1193 \times 0.327} = 3.87 \text{ L.}$$

This blood flow must be corrected, however, since the volume of air in the lungs (2.27 L.) has not been reduced to standard conditions and the mean tension of nitrous oxide (11.93 per cent) should be expressed in percentage of an atmosphere. Krogh finds that these two corrections counterbalance each other almost exactly leaving only a slight correction,¹⁵ dependent on the temperature, by which the above result must be multiplied. The above blood flow then becomes:

$$3.87 \times \frac{96}{100} = 3.72 \text{ L.}$$

According to the short method the entire calculation can be made as follows:

$$\frac{2.27 \times 0.0270 \times 0.96}{0.405 \times 0.1193 \times 0.327} = 3.72 \text{ L.}$$

¹⁵ Krogh: See reference 4.

The correction table as given by Krogh is as follows:

<i>Temp.</i>	<i>Correction</i>
14°	1.00
16°	0.99
18°	0.98
20°	0.97

From the above calculations it will be seen that this factor, though not absolutely correct, is sufficiently so for most purposes. For the ranges in temperature and pressure in our experiments the factor varies between $\frac{94}{100}$ and $\frac{99}{100}$. Krogh's table

does not allow for variations in the barometer, so that we have preferred to calculate all our experiments by the longer method.

Krogh states that the exactness of the experimental method allows determinations of the blood flow to be made within an error of 10 per cent. We believe this to be a very fair estimate of the accuracy of the method.

The nitrous oxide method of determining the blood flow, as has been pointed out above, possesses what may be considered as constant and accidental errors. The chief constant errors are inherent in the assumption that the blood, while passing through the lungs, reaches a condition of tension equilibrium with the nitrous oxide in the alveoli and that during the course of an experiment no appreciable amount of blood recirculates and enters the lungs for a second time. These errors, if they exist, cannot at the present time be obviated. The accidental errors also on account of the technical difficulties of the experiment may be numerous. We have attempted to reduce the influence of the accidental errors by performing a reasonably extensive series of experiments. We realize, however, that a much larger number would be highly desirable and regret that, for the present, stress of work on other lines prevents us from doing more experiments. We cannot, therefore, insist on the absolute accuracy of our blood flow data, though we believe the comparative figures can be considered as being reasonably correct. The theoretical venous carbon dioxide and oxygen ten-

sions, as calculated from our blood flow data, are obviously open to the same criticism. As a control, however, we have made a number of direct determinations of the venous carbon dioxide and oxygen tensions according to the method suggested by Christiansen, Douglas, and Haldane¹⁶ and they agree with the calculated results here given in a very satisfactory manner. We hope shortly to complete a sufficient series for publication.

The essential data with the calculated results of all our experiments are given at the end of the paper in Tables II, III, and IV. These results are averaged into groups and presented in a summarized form in Table I.

TABLE I

O ₂ CONSUMPTION PER MIN.	BLOOD FLOW PER MIN.	PULSE RATE PER MIN.	TOTAL VENTILATION AT 37° SAT. AT PREVAIL- ING BAR. PRESS. PER MIN.
cc.	L		L
175	3.37	58	5.5
185	3.57	58	6.7
320	5.06	75	9.8
448	5.30	87	12.8
559	6.54	96	15.5
608	7.59	91	16.8
912	9.31	133	24.1

Weight subject, 48 kilos.

The averages of the calculated results from Table I are plotted in Figure III in which the ordinates represent the volume or amount of the various factors and the abscissa is the oxygen consumption per minute expressed in cubic centimeters and at standard temperature and pressure dry. In Figure IV these curves are repeated with the addition of several secondary curves. An explanation and discussion of the construction of the curves in this figure follow.

I. Blood flow. The averages for the blood flow determinations show a progressive though slightly irregular increase with the oxygen consumption. We have constructed a straight line

¹⁶ Christiansen, Douglas, and Haldane: The absorption and dissociation of carbon dioxide by human blood. Jour. Physiol., 1914, xlviii, 4, 244-271.

to represent the increase in blood flow, as such a line passes nearer to all the plotted points than would a simple curve. From considerations elaborated fully on page 413 it is highly

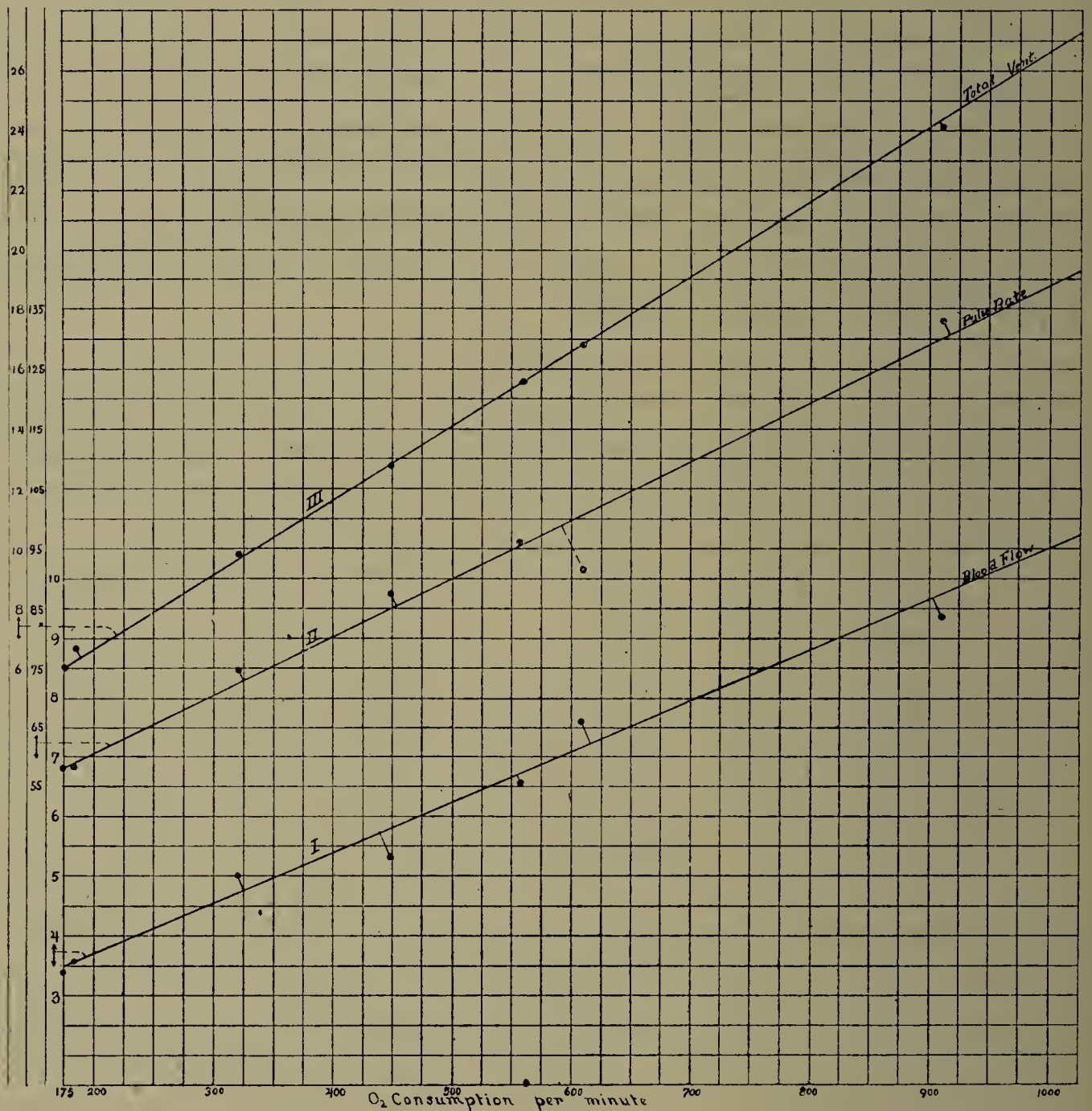


Fig. III. Curve I, blood flow. Curve II, pulse rate. Curve III, total ventilation. For description of curves see text. Ordinate represents litres per minute for blood flow; and total ventilation; and beats per minute for pulse rate. Abcissa is the oxygen consumption per minute in cubic centimeters.

probable that the blood flow follows some definite law of increase corresponding to its increased functions. The other two mechanical factors concerned with the transportation of the respiratory gases which are directly measurable are the total venti-

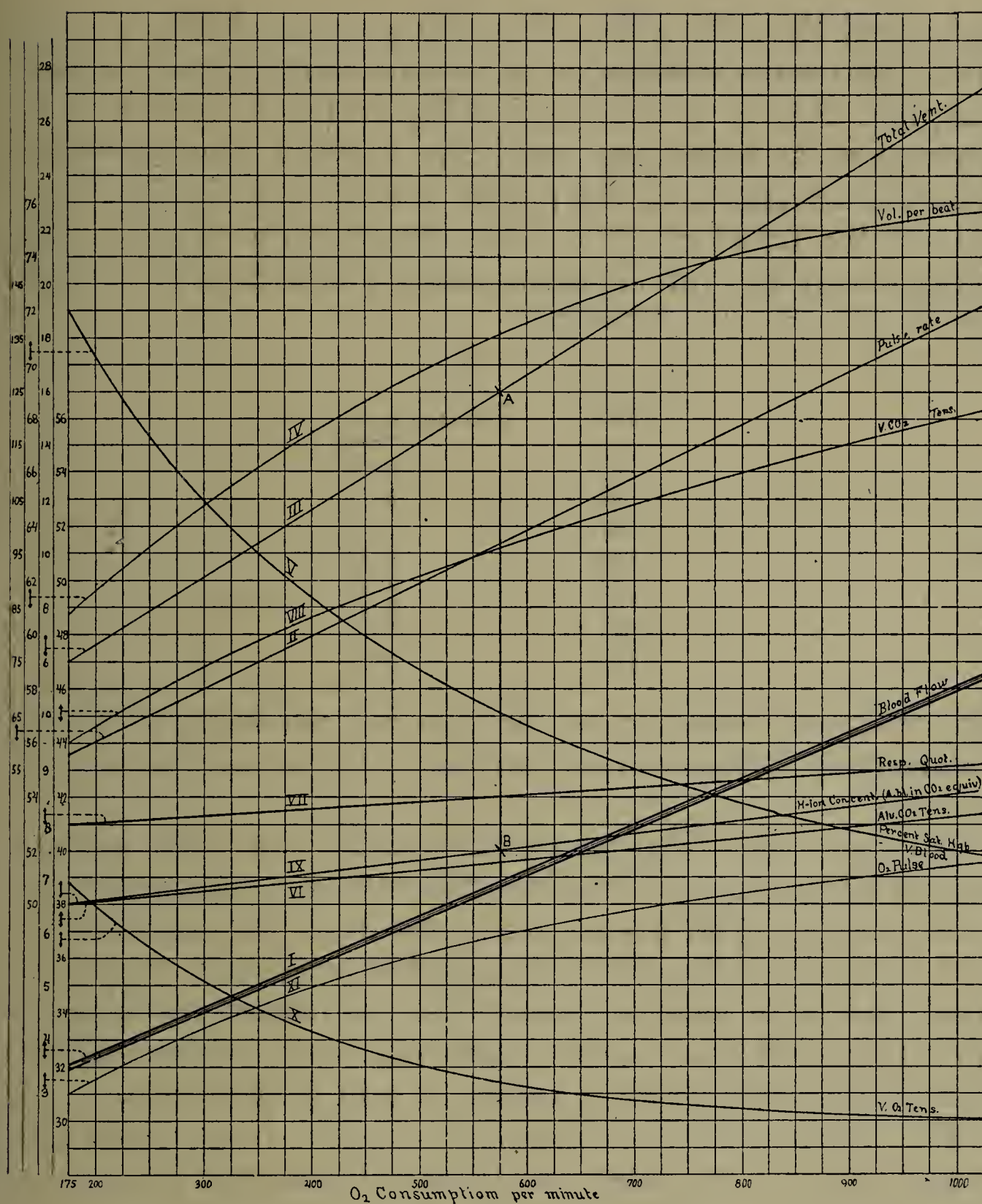


Fig. IV. Curves I, II, and III are the same as in the preceding figure, except that the plotted points representing the data are eliminated. The remaining curves are calculated from the three primary curves as described in text. Curve IV, volume per beat. Curve V, percentage saturation of the haemoglobin in the mixed venous blood. Curve VI, alveolar CO_2 tension. Curve VII, respiratory quotient. Curve VIII, tension of CO_2 in the venous blood, allowing for the influence of the percentage saturation of the haemoglobin with oxygen. Curve IX, hydrogen ion concentration of the arterial blood (for construction see text). Curve X, tension of oxygen in the venous blood allowing for the influence of the total acidity. Curve XI, oxygen pulse (Henderson).

lation and the pulse rate. From Curves II and III, it is seen that these factors increase, on the average, according to a straight line; that they do so lends probability to the correctness of the assumption on which the blood flow curve is constructed and that the divergence of the plotted points from the line is not beyond the limits of error of the experimental method. The divergence of the various experimental points from the straight line is shown by the following:

<i>Position of point cc.</i>	<i>Divergence from curve I per cent</i>
175	0.6
185	0.3
320	7.0
448	8.6
559	2.8
608	6.2
912	3.9

The values as found by us for man are consistent with those obtained by Patterson and Starling¹⁷ in their heart-lung preparations.

II. Pulse rate. The points representing the pulse rate fall within 3 per cent of a straight line with the exception of one corresponding to an oxygen consumption of 608 cc.; this point is 9 per cent off the line. It is evident, therefore, that in the main the pulse rate increases with the oxygen consumption, though in individual instances nervous or other influences may modify the rate somewhat, as can be seen in the tables.

III. Total ventilation. The various points representing total ventilation (37° saturated and existing barometer) likewise fall very close to a straight line with the exception of that corresponding to 185 cc. oxygen consumption. This may possibly be explained by the fact that the determination at 175 cc. was made with the subject lying down and that at 185 cc. was made while sitting in a chair. The change in position might have had an appreciable effect on the ventilation.

¹⁷ Patterson and Starling: On the mechanical factors which determine the output of the ventricles. Jour. Physiol., 1914. xlviii, 5, 357-380.

IV. Volume per beat. The curve representing the volume of blood pumped by the heart at each stroke was determined by dividing the volume per minute, as read from the blood flow curve, by the number of beats per minute, as shown by the pulse rate curve. This calculation was made for 175, 200, 300, 400, 500, 600, 700, 800, and 900 cc. of oxygen consumption. Likewise in the construction of the other secondary curves we have made the calculations directly from the primary curves and not from the actual experimental points. It is evident that the volume per beat increases at first quite rapidly and then very much more slowly.

In individual experiments the heart rate and the volume per beat vary inversely. The output per minute is, therefore, as Patterson and Starling¹⁸ show, probably dependent on the amount of blood flowing into the heart.

V. Percentage saturation of the haemoglobin. The percentage saturation of the haemoglobin in the venous blood can be calculated as follows. In the subject of these experiments the haemoglobin per cent is 120, as determined by the Haldane-Gower's haemoglobinometer. Within the limits of the work and under the conditions existing in the blood flow experiments, there was no appreciable change in the haemoglobin percentage of the subject whether at rest or at work. This fact, however, must be experimentally determined, because individuals vary greatly, as shown by Boothby and Berry.¹⁹ The amount of oxygen carried by a litre of fully saturated blood would then be $185 \times \frac{120}{100} = 222$; to which must be added 3.0 cc. in the plasma, making a total of 225 cc. However, Cook and Barcroft²⁰ have shown that the haemoglobin, as it leaves the lungs, is only 94 per cent saturated. Therefore the arterial blood con-

¹⁸ Patterson and Starling: On the mechanical factors which determine the output of the ventricles. *Jour. Physiol.*, 1914, xlviii, 5, 357-380.

¹⁹ Boothby and Berry: Effects of work on the percentage of haemoglobin and number of red corpuscles in the blood. *This Journal*, 1915, xxxvii.

²⁰ Cook and Barcroft: Direct determination of percentage saturation of the arterial blood with oxygen in a normal person. *Jour. Physiol.*, 1913, xlvii; *Proc. Phys. Soc.*, xxxv.

tains only 212 cc. of oxygen: $222 \times \frac{94}{100} = 212$ cc. The percentage saturation of haemoglobin in arterial blood during work has never been determined experimentally, so far as we know. We have been obliged, therefore, to use the same figure (212 cc.) for both rest and work, thus possibly introducing a slight error. For 300 cc. oxygen consumption per minute the oxygen per litre of blood is obtained by dividing by the blood flow (4.53 L.) $\frac{300}{4.53} = 66$ cc. If 66 cc. oxygen per litre is used then the venous blood contains $212 - 66 = 146$ cc. As the total oxygen capacity is 225 cc.²¹ then the percentage saturation of the venous blood is $\frac{146}{225} = 64.9$ per cent. The form of the percentage saturation curve is remarkably interesting and it illustrates the economical interrelationship of the various factors concerned in the body metabolism.

VI. The alveolar carbon dioxide tension. The points representing the alveolar carbon dioxide tension were in a few instances obtained in the circulation experiments. They were mostly obtained, however, by an independent study. The method in brief was to take alveolar air samples by the Haldane-Priestly method before beginning work and again about twenty minutes after commencing to work, by which time equilibrium was assumed to be established. Although there were exceptions both above and below, we obtained an average rise of 2 mm. in the alveolar carbon dioxide tension above the resting value, when work was done requiring 700 cc. of oxygen consumption per minute. Krogh and Lindhard²² have recently criticised the Haldane-Priestly samples under conditions of work as being likely to give too high a percentage for carbon dioxide and too low for oxygen. The error is due, according to them, to an extra

²¹ In this calculation we have assumed that the oxygen dissolved in the plasma behaves as though it were in combination with the haemoglobin. The error thus introduced is negligible.

²² Krogh and Lindhard: On the average composition of the alveolar air and its variations during the respiratory cycle. *Jour. Physiol.*, 1914, xlvii, 6, 431-445.

elimination of carbon dioxide and absorption of oxygen during the time necessary to make a complete expiration. The Haldane-Priestly alveolar samples do not, therefore, represent the true mean alveolar air tension. As near as can be judged from the curves given by Krogh and Lindhard for work in the region of 700 cc. oxygen consumption, the correction would be of the order of -1.0 mm. We have thought it best to make this arbitrary correction as it agrees with the results of some investigations that we have at present under way, though not yet ready for publication.

VII. Respiratory quotient. From the respiration experiments preceding the circulation experiments proper it is evident that the respiratory quotient increases from an average of about 0.8 at rest to about 0.9 at work requiring 900 cc. of oxygen consumption. This increase in the respiratory quotient may have an important metabolic significance or it may be due to a readjustment of the total amount of carbon dioxide stored in the body tissues. We will not now enter into a discussion of this point, as our data are not sufficient to determine such a fundamental process. For this paper it is of importance merely as providing a convenient method of calculating the carbon dioxide elimination per minute under various amounts of oxygen consumption. This is done by multiplying the oxygen consumption by the respiratory quotient.

VIII. The venous carbon dioxide tension. Christiansen, Douglas and Haldane²³ have recently determined the absorption curve of carbon dioxide for human blood and the variations produced on the carbon dioxide carrying capacity by the percentage saturation of the haemoglobin. In Figure 3 of their paper are given the curves for the absorption of carbon dioxide by the blood of J. S. H. in the presence of air (haemoglobin saturated) and in the presence of hydrogen (haemoglobin desaturated). They assume that the line *AB* represents the absorption of carbon dioxide by the blood of J. S. H. within the body at rest on the ground that "if the blood were completely reduced and

²³ Christiansen, Douglas and Haldane: The absorption and dissociation of carbon dioxide by human blood. Jour. Physiol., 1914, xlviii, 4, 244-271.

a corresponding formation of carbon dioxide occurred, the rise of carbon dioxide would only amount to 22 mm." We reproduce their figure in our Figure V with the addition of lines interpolated to indicate the probable effect of the haemoglobin at 50, 55, 60, 65, 70, and 94 per cent saturation. The formation of the line $A'B'$ will be described presently.

The venous carbon dioxide tension, with allowance for the effect of the percentage saturation of the haemoglobin, can be determined in the following way. For an oxygen consumption of 500 cc. the alveolar carbon dioxide tension is 39.35 mm. (Curve VI, Fig. IV) at which tension the blood contains 51.4 volumes of carbon dioxide (Fig. V, haemoglobin 94 per cent sat.). The respiratory quotient is 0.845 (Curve VII, Fig. IV), therefore the carbon dioxide elimination per minute is $500 \times 0.845 = 423$ cc. per minute. The blood flow per minute is 6.26 L. (Curve I, Fig. IV), therefore each litre of blood carries to the lungs for elimination $\frac{423}{6.26} = 67.6$ cc. of carbon dioxide.

In consequence each litre of the venous blood must have contained $51.4 + 6.76 = 58.16$ volumes. As the haemoglobin is 58.7 per cent saturated (Curve V, Fig. IV), the tension at which the carbon dioxide must be for the blood to contain 58.16 volumes is found from Figure V to be 50.1 mm.

In Figure V the place at which the line representing the volume of carbon dioxide absorbed by the blood crosses the line representing the percentage saturation of the haemoglobin has been marked with a large black dot. The points representing the various amounts of oxygen consumption have been connected by the line $A'B'$. The line $A'B'$ therefore represents the absorption of carbon dioxide within the body of W. M. B. under a progressively increasing oxygen consumption per minute; it starts at point A' instead of point A , as the alveolar carbon dioxide tension of W. M. B. is 38 mm. instead of 40 mm. as is the case for Dr. Haldane. The first part of the line $A'B'$ is nearly parallel to the line AB ; it then quickly curves to the right and crosses the line AB . Christiansen, Douglas, and Haldane predict that under conditions of work there will be a displace-

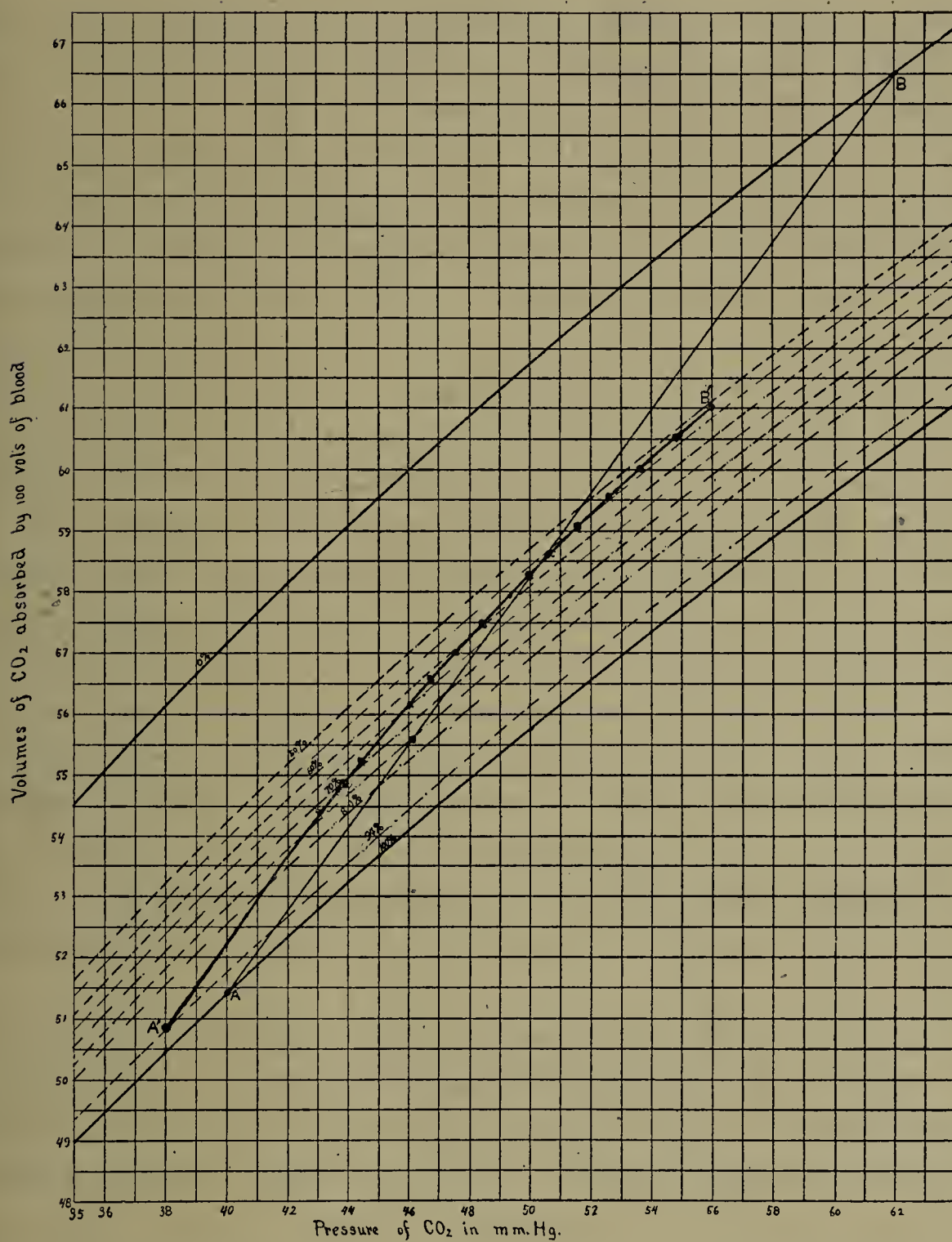


Fig. V. Enlarged section of Figure 3 from paper of Christensen, Douglas, and Haldane, Jour. Physiol., 1914, xlviii, 4, p. 259. "The upper solid line represents absorption of CO_2 by blood of J. S. H. in presence of hydrogen (Hgb. de-saturated). Lower solid line represents absorption of CO_2 by blood of J. S. H. in presence of air (Hgb. saturated). The line AB represents the absorption of CO_2 by the blood of J. S. H. within the body." The intermediate dotted lines are interpolated by us to represent the partial degrees of saturation of the haemoglobin with O_2 . The line $A'B'$ represents the absorption of CO_2 by the blood of W. M. B., as determined from our experiments. Ordinate represents volumes of CO_2 reduced to 760 mm. and 0° dry, absorbed by 100 volumes of blood at 37° . Abscissa represents the pressure of CO_2 in mm. of Hg.

ment of the line to the right by saying that "during any exertion the difference between arterial and venous carbon dioxide pressure appears to increase very greatly."

The curve representing the venous carbon dioxide tension, however, can only be considered as approximately correct as the absorption curves for carbon dioxide have never been determined for the blood of W. M. B. The error is probably not great and would be of the same order throughout the series.

IX. Hydrogen ion concentration of the arterial blood. In 1905 Haldane and Priestly²⁴ showed that under normal conditions the breathing is so regulated as to maintain in each individual a practically constant partial pressure of carbon dioxide in the alveolar air. So delicate is the regulation that, other things being equal, a rise of 1 mm. of carbon dioxide pressure increases the breathing by about 80 per cent. Boycott and Haldane²⁵ in 1908 showed that the action on the respiratory centre of the circulating blood is due to what they called its "total acidity," comprising the free carbon dioxide and some other acid, presumably lactic acid. Hasselbalch²⁶ has recently shown that these combined acids affect the centre according to the concentration of the hydrogen ions which they produce in the arterial blood.

Campbell, Douglas and Hobson²⁷ have recently reviewed the earlier experiments of Haldane and Priestly and of Campbell, Douglas, Haldane and Hobson²⁸ and have carried out further and more exact experiments. They find that "the rise of alveo-

²⁴ Haldane and Priestly: The regulation of the lung ventilation. *Jour. Physiol.*, 1905, xxxii, 225-266.

²⁵ Boycott and Haldane: The effects of low atmospheric pressures on respiration. *Jour. Physiol.*, 1908, xxxvii, nos. 5 and 6, 355-377.

²⁶ Hasselbalch: Neutralitätsregulation und Reizbarkeit des Atemzentrums in ihren Wirkungen auf die Kohlensäurespannung des Blutes. *Biochem. Ztschft.* 1912, xlvi, 404-439.

²⁷ Campbell, Douglas, and Hobson: The sensitiveness of the respiratory centre to carbonic acid, and the dead space during hyperpnoea. *Jour. Physiol.* 1914, xlviii, 4, 303-316.

²⁸ Campbell, Douglas, Haldane, and Hobson: The response of the respiratory centre to carbonic acid, oxygen, and hydrogen ion concentration. *Jour. Physiol.*, 1913, xlvi, 301-318.

lar carbon dioxide pressure, (other acids remaining constant), required to give a rise of 10 litres in the alveolar ventilation was 2.5 mm. and in the total ventilation 2.0 mm.; that is, a rise in the carbon dioxide percentage in the dry alveolar air of 0.35 per cent and 0.28 per cent. Judging from Hasselbalch and Lundsgaard's results these figures would imply a rise in the C_H in the arterial blood of about 0.0163×10^{-7} and 0.013×10^{-7} respectively."

These figures obtained in the experiments of Campbell, Douglas, and Hobson are in close agreement with those obtained in earlier experiments with Haldane. The subject (W. M. B.) of the circulation experiments here reported was one of the subjects from which this average figure was obtained by Campbell, Douglas, Haldane, and Hobson. Therefore the sensitiveness of the respiratory centre of W. M. B. is known to agree closely with the figures given above.

Such being the case we can construct Curve IX of Figure IV to represent the hydrogen ion concentration of the arterial blood by dropping a perpendicular line from point A on Curve III, which represents an increase of 10 litres in the total ventilation, and running Curve IX through point B which is 2.0 mm. above the resting alveolar carbon dioxide tension. The difference between Curves VI and IX is a measure in terms of carbon dioxide, of the amount of lactic acid in the blood under various degrees of work. It is to be noted that severe work, such as could be maintained only for a brief period, was not performed. Work causing an oxygen consumption of 900 cc. was, however, the maximum that could be maintained with reasonable comfort for one and one-half hours; at the end the subject was glad to be through the experiment but was in no way exhausted or "all in."

X. Venous oxygen tension. The tension at which the oxygen will be present for a given percentage saturation, will depend on the total acidity of the blood. The total acidity of the venous blood can be estimated by taking the carbon dioxide equivalent of the lactic acid, found by subtracting points on Curve VI from corresponding points on Curve IX, and adding

it to corresponding points on Curve VIII. Knowing the total acidity the oxygen tension of the venous blood for any degree of saturation can be read directly from the dissociation curve for oxygen given in Figure VI. Thus for 500 cc. oxygen consumption the difference between Curves VI and IX, representing the lactic acid, is 0.35 mm. The corresponding point on Curve VIII, for the venous carbon dioxide tension, is 50.1 mm. and the total acidity is, therefore, $50.1 + 0.35 = 50.45$ mm. The percentage saturation of the haemoglobin for 500 cc. oxygen consumption is 58.7 per cent (Curve V, Fig. IV) and the oxygen tension corresponding to 50.45 mm. of carbon dioxide at this percentage saturation is 32.2 mm.

No direct determinations of the oxygen dissociation curves of Boothby's blood have been made except at 40 mm. carbon dioxide pressure. At this carbon dioxide pressure it is known, however, to agree quite closely with that of Barcroft's blood.²⁹ Barcroft³⁰ gives the dissociation curves for his own blood at 20, 40, and 90 mm. carbon dioxide pressure. In Figure VI we have reproduced his figure, enlarged the scale somewhat, and interpolated dotted lines to approximately indicate the intermediate carbon dioxide tensions. The interpolation, though not absolutely correct, is sufficiently accurate for the comparative purposes of this paper.

The heavy line *AB* in Figure VI represents the curve of oxy-haemoglobin in the blood of W. M. B. within the body and is constructed by connecting the points made by the crossing of the lines representing the percentage saturation with those representing the total acidity of the venous blood in terms of carbon dioxide. It shows that the influence of the total acidity of the blood within the body is of considerable moment and of a distinctly larger order than is thought probable by Christiansen, Douglas, and Haldane. The discrepancy is accounted for by the fact that their calculation, (shown in their Fig. 4), is merely based on one point which was determined at rest, while ours is

²⁹ Barcroft: The respiratory function of the blood. 1914, University Press, Cambridge, England, p. 219.

³⁰ Barcroft: loc. cit., p. 65, fig. 34.

founded on data obtained not only at rest but also with progressively increasing amounts of work. It is possible that even a greater change in the dissociation curve of oxyhaemoglobin would be produced under conditions of prolonged oxygen want such as exists at high altitudes.

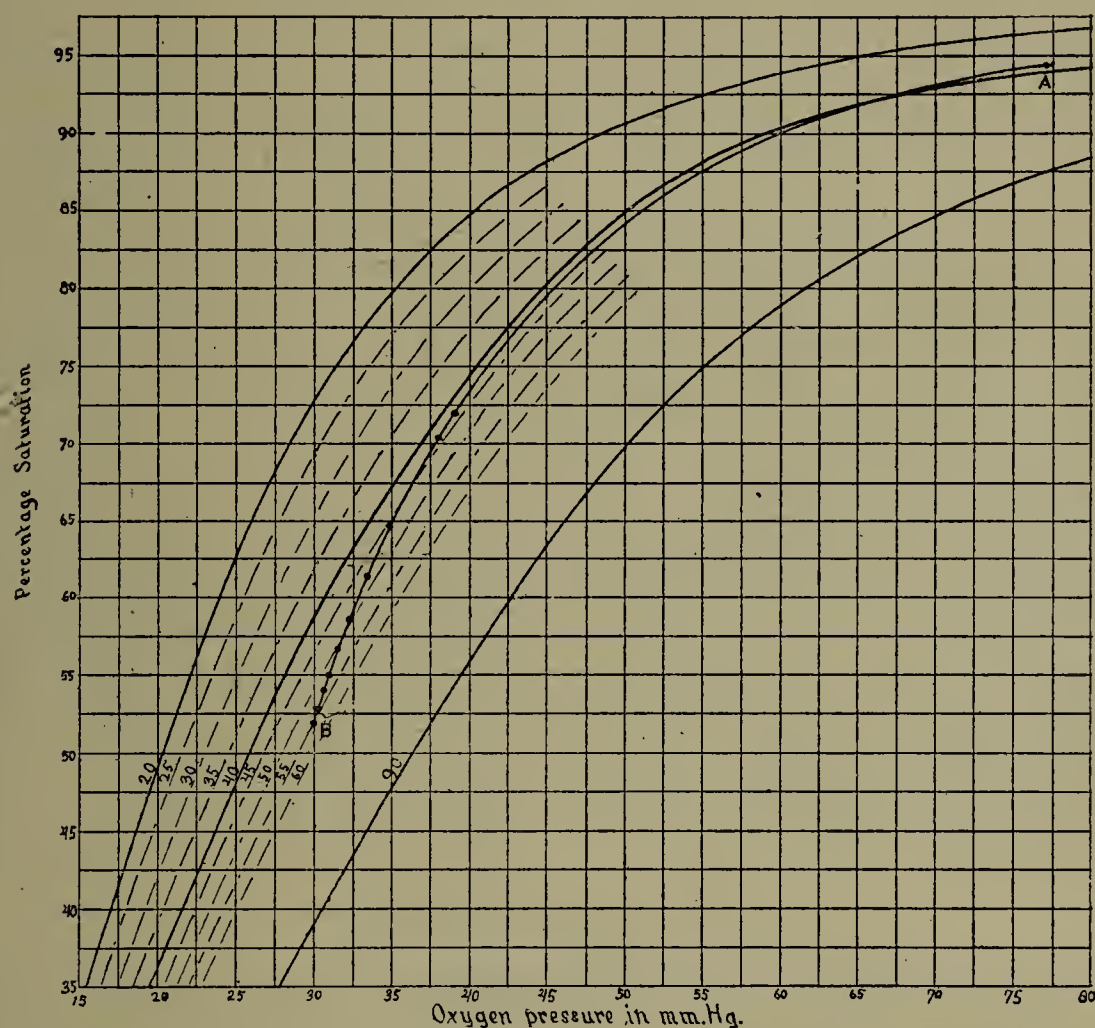


Fig. VI. Enlarged section of Figure 34, p. 65 in Barcroft's book on The Respiratory Function of the Blood. The heavy lines represent the dissociation curve of Barcroft's blood at 20, 40, and 90 mm. CO_2 . The dotted lines are interpolated by us to represent the probable effect of the intermediate CO_2 tensions. The line *AB* represents the dissociation curve of the haemoglobin of the blood of W. M. B. within the body. Ordinate represents percentage saturation. Abcissa represents oxygen pressure.

XI. Oxygen pulse. Henderson and Prince³¹ have recently introduced the very useful term "oxygen pulse" to represent the amount of oxygen consumed by the body from the blood of one systolic discharge of the heart. Curve XI in Figure IV repre-

³¹ Henderson and Prince: The oxygen pulse and the systolic discharge. Amer. Jour. Physiol., 1914, xxxv, 106-115.

sents the oxygen pulse in our series of experiments and is obtained by dividing the oxygen consumption per minute by the pulse rate.

From the oxygen pulse Henderson and Prince attempt to estimate the probable systolic discharge by computing on the basis "that the heart under normal conditions obeys the principle of 'superimposability of the volume curve.' " On this assumption values are obtained which are quite at variance with ours. The curves for "superimposability" were obtained on dogs and cats with the thorax open and with the animals at rest. To us it does not seem permissible to extrapolate these curves to conditions of severe work and then make use of them for calculating the systolic output of the heart of normal man.

Although Henderson's³² calculated results for the systolic output are so divergent from ours, as well as from those of Nicolai and Zuntz,³³ yet the experimental data³⁴ itself appears consistent with our findings, if it is realized that the increase in the heart rate was due in his experiments to other causes than that of increased work with the development of the need of a greater gaseous carrying capacity of the blood per minute.

DISCUSSION OF RESULTS

The experimental evidence here offered shows that the circulation rate increases progressively with the oxygen consumption per minute in a manner corresponding to the increase in the total ventilation.

Respiration consists of various factors the chief of which are: (1) the ventilation of the lungs; (2) the passage of gases through the lung epithelium to and from the blood; (3) the transportation of gases to and from the tissues; (4) cell respiration.

³² Henderson: The law of the systolic discharge. Internat'l Physiolog. Congress, Vienna, 1910.

³³ Nicolai and Zuntz: Fullung und Entleerung des Herzens bei Ruhe und Arbeit. Berl. klin. Wchusch, 1914 (Nov. 18).

³⁴ Henderson: The volume curve of the ventricles of the mammalian heart and the significance of this curve in respect to the mechanics of the heart beat and filling of the ventricles. Amer. Jour. Physiol., 1906, xvi, 325-366.

The respiratory function of the lungs and of the blood is absolutely identical in a true physiological and biological sense. On account of the physical and mechanical problems involved there must, however, be two distinct carrying devices provided for getting the gases from the air to and from the cells.

It is difficult to believe that one part of this respiratory mechanism—the ventilation of the lungs—is carefully and delicately regulated to the needs of the body without the other mechanism—the circulation of the blood—being likewise as carefully and delicately regulated.

It is further highly probable that the same factor which regulates and controls respiration governs both these mechanical processes—the ventilation of the lungs and the circulation of the blood—and not merely one of them as heretofore believed.

On these grounds we feel justified in assuming that the same regulatory factor—the hydrogen ion concentration of the arterial blood—controls with equal delicacy the ventilation of the lungs and the rapidity of the circulation rate.

This conception is strengthened by the evidence given in a previous article³⁵ in which we showed that after forced breathing—which produces a reduction in the arterial carbon dioxide tension with a parallel decrease in the hydrogen ion concentration—the circulation rate is slowed.

If we assume that the same regulatory factor governs both processes, it is only necessary to show a correspondence between the two processes to estimate the delicacy and sensitiveness of what may be looked upon as a “centre” governing the circulation rate. From what has been said above, it is possible that the “circulatory centre” is really only a part of the respiratory centre. Also that the centre hitherto considered as the respiratory centre is best considered as a ventilation centre. The respiratory centre can then be thought of as a large centre composed of subordinate centres of which we consider here only the sub-centres controlling pulmonary ventilation and circulation rate.

³⁵ Boothby: Absence of apnoea after forced breathing. *Jour. Physiol.*, 1912, xlv, 5, 328-337.

In addition to the chemical regulation of the circulation it is evident that it can be influenced by factors of nervous or psychic origin in the same manner as in the pulmonary ventilation. Our experiments indicate that such influences, however, are only temporary and designed to meet sudden emergencies which require immediately in the muscles a greatly increased oxygen supply before a sufficient time could elapse for the chemical stimulus to be produced and to take effect.

SUMMARY

I. The experimental details as used by us are given for determining the blood flow according to the method of Krogh and Lindhard.

II. A series of sixty-one determinations of the blood flow in one subject at rest and at various degrees of work are reported.

III. By these experiments it is shown that the circulation rate increases proportionately with the oxygen consumption in a manner corresponding to the increase in the total ventilation.

IV. It is suggested that the main controlling factor in the regulation of the circulation rate is the hydrogen ion concentration of the arterial blood and that this regulation is one of great delicacy.

V. By comparing the increase in the circulation rate with the increase in the total ventilation we are able to estimate that on the subject studied an increase in the blood flow of 3.3 litres per minute, which is a doubling of the circulation rate, is caused by a rise in the total acidity of the blood corresponding to 2.0 mm. of carbon dioxide. As pointed out by Campbell, Douglas, and Hobson, it is possible to deduce from the results of Hasselbalch and Lundsgaard that this figure would correspond to a rise in the hydrogen ion concentration of the arterial blood of about 0.013×10^{-7} .

TABLE II
Circulation experiments—subject lying at rest

EXPERIMENT NO.	DATE	ELEMENTS OF EXPERIMENT										BLOOD FLOW DATA						VALUES REDUCED TO NORMAL TO EXCHANGE									
		Bar. (corr.)		Temp. spir.	Length introd. period	Length experi-ment period	Initial volume	Final volume	Spirometer experiment				Sample I			Sample II			O ₂ absorbed per min.	Blood flow per	Pulse	Vol. per beat	O ₂ per litre blood	Vol. per pulse			
		1	2	3	4	5	6	7	8	R. Q.	Ventilation per min. at 37°	Pulse	O ₂	N ₂ O	N ₂	O ₂	N ₂ O	N ₂									
1	May 6	750.3	20.8°	10.1	20.2	2.38	2.28	150	183	0.82	5.78	57	14.13	13.42	67.79	11.86	11.47	70.70	175	3.30	52.2	63	22	23.12	24	53	61
2	May 6	750.3	20.8°	12.0	23.7	2.01	1.90	150	183	0.82	5.78	57	13.63	12.00	69.25	10.50	9.92	73.40	168	2.90	51.4	56	20	23.12	24	58	55
3	May 7	756.5	21.8°	11.2	21.0	2.31	2.20	136	159	0.86	5.24	56	14.29	12.86	68.10	11.97	10.45	71.62	171	3.90	52.6	74	19	23.12	24	44	65
4	May 7	756.5	21.8°	11.5	23.8	2.50	2.37	136	159	0.86	5.24	56	14.01	13.42	67.37	11.51	11.37	71.09	175	3.19	51.3	62	22	23.12	24	55	52
5	May 9	752.9	21.8°	9.7	19.8	2.10	2.00	161	189	0.85	6.03	61	14.56	12.41	68.36	11.77	10.32	71.63	190	3.43	57.4	60	22	23.12	24	55	56
6	May 9	752.9	21.8°	9.4	19.7	1.89	1.80	161	189	0.85	6.03	61	14.35	12.33	68.65	11.52	10.06	72.11	174	3.36	56.5	59	22	23.12	24	52	60
7	May 9	752.5	21.8°	10.4	19.6	2.27	2.17	140	171	0.82	5.01	58	14.52	13.05	68.06	12.14	10.81	71.09	181	3.75	56.0	67	22	23.12	24	48	61
8	May 9	752.5	21.8°	12.7	18.3	1.97	1.88	140	171	0.82	5.01	58	14.22	13.16	68.06	11.65	11.00	71.37	179	3.38	55.8	61	22	23.12	24	53	55

TABLE III

Circulation experiments—subject sitting at rest

EXPERIMENT NO.		ELEMENTS OF EXPERIMENT										BLOOD FLOW DATA				VALUES REDUCED TO NORMAL EXCHANGE										
		DATE		1	2	Length introd. period	4	Initial volume	6	Spirometer experiment				Sample I			Sample II			O ₂ absorbed per min.	Blood flow per min.	Pulse	Vol. per beat	O ₂ per litre blood	Vol. per pulse	
										CO ₂ per min.	O ₂ per min.	R. Q.	Ventilation per min. at 37°	Pulse	O ₂	N ₂ O	N ₂	O ₂	N ₂ O							N ₂
		Bar. (corr.)	Temp. spir.	3	secs.	litres	litres	cc.	cc.	8	9	10	litres	11	per cent	per cent	per cent	per cent	18	19	20	21	cc.	litres	cc.	cc.
1	Mar. 25	755.8	18.8°	8.0	24.0	3.32	3.24	(185)							16.27	6.90	72.98	13.83	215	3.46		21		(2.98)	(62)	
2	Mar. 25	755.8	18.8°	7.2	21.0	3.03	2.96	(185)							15.82	9.40	71.03	13.92	180	3.59				(3.69)	(50)	
3	Mar. 26	767.6	18.9°	9.8	21.1	3.03	2.95	(185)							15.30	9.10	71.42	13.44	176	3.18				(3.34)	(55)	
4	Mar. 30	761.5	19.1°	10.2	20.2	2.81	2.75	(185)							15.96	8.06	72.24	13.81	187	3.74				(3.70)	(50)	
5	Mar. 30	761.5	19.1°	9.8	20.6	2.23	2.15	(185)							15.54	8.89	71.46	12.73	195	3.38				(3.21)	(58)	
6	Apr. 3	755.7	16.9°	8.0	22.1	2.34	2.21	(185)							15.04	11.11	69.72	11.00	271	4.26				(2.91)	(64)	
7	Apr. 3	755.7	16.9°	10.3	17.6	2.73	2.65	(185)							15.15	10.32	70.40	12.51	257	3.00				(2.16)	(86)	
8	Apr. 8	757.8	18.1°	7.8	25.0	2.85	2.72	(185)							15.88	9.94	70.53	12.72	234	4.88				(3.86)	(48)	
9	Apr. 9	752.7	21.2°	11.2	19.6	3.21	3.15	(185)							14.64	12.72	68.63	12.59	198	1.61	56.7	28		(1.50)	(123)	
10	Apr. 10	761.5	19.5°	10.4	13.9	2.80	2.72	(185)							14.61	12.69	68.46	13.33	183	5.55	55.0	101		(5.61)	(33)	
11	Apr. 10	761.5	19.5°	9.7	13.3	2.67	2.61	(185)							14.93	11.92	69.10	13.57	183	4.15	54.5	76		(4.20)	(44)	
12	Apr. 14	768.2	21.5°	10.2	17.8	2.44	2.35	(185)							14.97	11.17	69.78	12.65	209	4.42	55.9	79		(3.91)	(47)	
13	Apr. 14	768.2	21.5°	9.0	18.9	2.32	2.21	(185)							14.66	13.23	68.09	12.08	211	4.27	56.1	76		(3.74)	(49)	
14	Apr. 15	766.9	20.5°	10.4	22.4	2.36	2.26	(185)							14.11	13.56	68.07	11.70	168	3.32	55.9	59		(3.66)	(51)	
15	Apr. 15	766.9	20.5°	10.0	21.9	2.31	2.19	(185)							14.32	12.82	68.48	11.39	203	3.73	59.7	62		(3.40)	(54)	
16	Apr. 15	766.9	20.5°	10.1	20.8	2.35	2.25	(185)							14.15	13.48	67.97	11.19	213	3.04	59.3	51		(2.64)	(70)	
17	Apr. 16	751.6	19.6°	9.0	24.1	2.15	2.01	(185)							14.30	13.41	68.01	11.04	192	4.40	50.2	88		(4.24)	(44)	
18	Apr. 17	757.8	19.6°	9.7	21.3	2.50	2.36	(185)							14.19	14.42	67.05	11.38	221	4.67	58.7	80		(3.91)	(47)	
19	Apr. 17	757.8	19.6°	9.9	22.6	2.51	2.37	(185)							14.38	14.15	67.25	11.56	210	4.23	57.1	74		(3.73)	(50)	
20	Apr. 22	759.1	22.0°	10.2	23.2	2.58	2.47	149	189	0.79	6.75	59			14.50	13.99	67.53	12.33	162	3.80	54.8	69		4.43	43	75
21	Apr. 22	759.1	22.0°	10.5	25.0	2.51	2.38	149	189	0.79	6.75	59			14.29	15.69	66.18	11.92	162	3.49	54.0	65		4.07	46	69
22	Apr. 23	765.8	21.7°	10.0	24.2	2.52	2.41	136	176	0.77	6.30	58			14.54	11.98	69.01	12.14	167	3.55	52.2	68		3.74	47	64
23	Apr. 23	765.8	21.7°	11.4	25.1	2.53	2.42	136	176	0.77	6.30	58			14.27	13.85	67.66	12.11	148	3.16	48.5	65		3.76	47	65
24	Apr. 23	765.8	21.7°	10.4	24.6	2.59	2.49	136	176	0.77	6.30	58			14.45	13.54	67.94	12.23	154	2.83	50.5	56		3.23	55	56
25	Apr. 24	767.4	20.5°	9.5	25.5	2.66	2.54	148	188	0.79	6.96	58			14.58	13.23	68.09	12.26	165	3.27	53.8	61		3.73	50	64
26	Apr. 24	767.4	20.5°	10.3	21.1	2.50	2.40	148	188	0.79	6.96	58			14.10	13.62	67.94	11.98	169	3.13	53.3	59		3.48	54	60

EXPERIMENT NO.	ELEMENTS OF EXPERIMENT											BLOOD FLOW DATA				VALUES REDUCED TO NORMAL EXCHANGE									
	DATE	1 Bar. (corr.)	2 Temp. spir.	Length introd. period	4 Length experi-ment period	5 Initial volume litres	6 Final volume litres	Spirometer experiment				Sample I			Sample II			O ₂ absorbed per min.	Blood flow per min.	Pulse	Vol. per beat				
								CO ₂ per min.	O ₂ per min.	R. Q.	Ventilation per min. at 37°	Pulse	O ₂	N ₂ O	N ₂	O ₂	N ₂ O					N ₂			
		cc.	cc.	secs.	secs.	litres	litres	cc.	cc.	litres	litres	litres	per cent	per cent	per cent	per cent	per cent	per cent	cc.	litres	cc.	cc.	O ₂ per litre blood	Vol. per pulse	
1	June 4	758.6	21.0°	10.1	20.8	2.35	2.35	225	284	0.79	9.24	65	22.62	13.67	59.76	18.86	11.57	63.50	319	3.81	57.6	66	3.39	84	52
2	June 4	758.6	21.0°	9.9	17.8	2.30	2.18	225	284	0.79	9.24	65	19.59	13.88	62.63	16.07	11.95	66.02	306	3.65	58.1	63	3.39	84	52
3	June 5	758.6	20.0°	9.1	24.2	2.69	2.50	261	313	0.83	10.0	81	16.25	16.51	62.88	12.54	13.36	67.78	279	4.38	63.7	69	4.91	64	61
4	June 5	758.6	20.0°	10.3	24.3	2.62	2.46	261	313	0.83	10.0	81	17.07	14.31	64.31	13.49	11.79	68.52	259	3.85	62.7	61	4.65	67	57
5	June 10	769.3	20.5°	10.6	25.1	2.77	2.58	270	322	0.84	10.0	72	17.78	13.80	63.83	13.54	11.29	68.49	314	4.14	59?	70?	4.25	76	59
6	June 10	769.3	20.5°	10.2	23.3	2.49	2.32	270	322	0.84	10.0	72	17.53	14.38	63.57	13.52	11.75	68.21	290	4.01	54?	74?	4.45	72	62
7	June 2	762.1	21.5°	10.7	18.0	2.49	2.35	277	328	0.84	10.1	86	13.73	15.11	66.35	11.16	12.34	70.33	240	4.96	65.1	76	6.78	48	79
8	June 2	762.1	21.5°	9.0	20.5	2.72	2.57	277	328	0.84	10.1	86	13.97	15.57	66.10	11.14	12.71	70.03	248	4.75	68.7	69	6.28	52	73
9	June 2	761.9	23.0°	12.2	19.3	2.55	2.42	269	329	0.82	9.72	78	13.16	14.63	67.30	10.60	12.36	70.83	221	4.02	59.3	68	5.98	55	77
10	June 2	761.9	23.0°	10.4	20.9	2.50	2.36	269	329	0.82	9.72	78	13.87	14.84	66.88	10.55	12.29	70.93	252	4.05	60.0	67	5.29	62	68
11	May 26	761.2	24.0°	9.5	15.6	2.61	2.48	261	331	0.79	9.37	73	14.21	14.26	67.37	11.35	11.80	70.85	307	5.51	59.6	92	5.94	56	81
12	May 29	772.8	21.0°	9.6	24.8	2.61	2.43	258	333	0.78	10.2	68	13.97	14.60	67.22	9.98	11.59	72.34	272	4.38	57.3	76	5.36	62	79
13	June 22	760.5	21.5°	12.3	16.2	2.66	2.50	372	443	0.84	12.2	86	17.35	13.26	64.43	13.32	11.37	63.45	430	4.89	74.0	66	5.04	88	59
14	June 22	760.5	21.5°	9.3	16.1	2.42	2.27	372	443	0.84	12.2	86	18.37	13.08	63.97	14.01	10.92	68.20	426	5.06	75.0	67	5.26	84	61
15	June 11	755.7	23.0°	9.7	18.2	2.61	2.43	388	452	0.86	13.3	87	17.15	13.22	64.64	12.63	10.92	69.38	414	5.14	70.6	73	5.61	81	64
16	June 15	758.1	20.7°	7.0	12.4	2.55	2.40	476	554	0.86	15.5	97	17.77	12.93	64.62	13.43	10.83	68.79	572	6.76	75.0	91	6.58	84	68
17	June 15	758.1	20.7°	8.1	13.5	2.41	2.24	476	554	0.86	15.5	97	19.00	14.29	62.06	14.39	12.01	66.71	544	6.08	79.7	76	6.19	90	64
18	June 18	764.2	22.0°	9.2	11.4	2.39	2.24	494	563	0.88	15.4	94	16.92	12.44	65.21	12.67	10.50	69.48	575	6.76	80.8	84	6.62	85	70
19	June 18	764.2	22.0°	8.7	14.4	2.47	2.29	494	563	0.88	15.4	94	18.20	14.09	62.57	13.64	11.65	67.52	518	6.24	77.4	81	6.78	83	72
20	June 16	754.7	20.5°	8.7	13.2	2.32	2.15	542	608	0.89	16.8	91	17.23	14.06	63.53	12.83	11.45	68.45	507	6.80	78.3	87	8.16	75	90
21	June 16	754.7	20.5°	9.4	12.9	2.72	2.56	542	608	0.89	16.8	91	17.75	13.43	63.55	13.75	11.50	67.60	547	6.31	79.3	80	7.01	87	77
22	June 12	755.1	25.0°	6.7	8.7	2.51	2.34	821	909	0.90	24.5	140	17.83	12.31	64.51	13.08	10.30	69.27	860	9.69			10.24	89	73
23	June 25	755.6	27.8°	6.8	7.4	2.56	2.40	842	912	0.92	24.2	130	17.27	14.04	63.24	13.14	12.07	67.39	883	9.94	133	75	10.15	90	78
24	June 25	755.6	27.8°	5.7	7.9	2.40	2.28	842	912	0.92	24.2	130	17.22	14.22	63.26	12.54	13.36	66.71	838	4.62	127	36	5.03	181	39*
25	June 23	760.6	23.2°	6.1	8.1	2.43	2.29	831	914	0.91	23.1	129	18.00	13.48	63.29	13.55	11.78	67.16	845	8.00	126	64	8.65	106	67
26	June 24	758.9	25.0°	8.8	8.2	2.80	2.66	863	914	0.94	24.4	133	17.27	12.91	64.38	13.15	11.67	67.77	868	7.10	124	57	7.48	122	56
27	June 24	758.9	25.0°	6.5	7.2	2.69	2.54	863	914	0.94	24.4	133	17.49	12.81	64.10	13.76	11.19	67.78	893	9.79	131	75	10.02	91	75

* Exp. 24 omitted in the averages.

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